

## **REMARKS**

### **Drawings**

Transmitted herewith is Substitute Figures, for filing in the subject patent application. The margins of the drawing sheets have been corrected in order to comply with 37 C.F.R. § 1.84(g). Applicants assert that no new matter is presented by these amendments and respectfully request entry of the same.

### **Specification**

The specification has been amended to address the Examiner's objections and typographical errors. Specifically, embedded hyperlink on page 30 has been deleted.

The specification has also been amended add Sequence ID Numbers, a paper copy and computer readable of a sequence listing with the corresponding statement as required by C.F.R. § 1.821 is enclosed with this amendment. Applicants assert that no new matter is presented by these amendments and respectfully request entry of the same.

### **Claim Objections**

Claim 4 and 5 have been amended to address the Examiner's objections. Specifically, a space has been added between "3" and "wherein". Applicants assert that no new matter is presented by these amendments and respectfully request entry of the same.

### **Claim Rejections – 35 USC § 112**

Claims 1-15 and 45-59 are rejected under 35 USC 112 second paragraph, as allegedly being in definite. Applicant respectfully disagree.

The Office Action alleges that the method steps set forth in Claim 1 are directed to the selection of a single probe. Applicant has amended the claim to recite “selecting the candidate probes.” Therefore, this claim rejection is obviated.

The Office Action alleges that it is not clear as to what type of data should be used in the equation in Claim 2. Applicant respectfully submits that the two types of data,  $P_i$  (parameters) and the functionals ( $S_i$ ) are clearly indicated in the claim are told in great detail in the specification, for example, from pages 17-21. The Office Action also seems to be confused about what the result of the prediction. The result of the prediction is the probe hybridization intensity. The sequence of a potential probe is given. Therefore, the scope of the claim is clear and this rejection should be withdrawn.

Claim 3 is rejected for allegedly being indefinite for reciting “functional of said sequence.” The specification teaches in great detail about the functionals  $S_i$  (for example, page 18, line 3-5, page 21, line 1). The functional  $S_i$  is a value derived from the probe sequence. From page 18 to page 22, for example, the specification teaches the exemplary relationship between  $S_i$  and the probe sequence. Therefore, Applicant respectfully submits that this rejection of Claim 3 should be withdrawn.

Claim 5 is rejected for allegedly being indefinite for reciting “ $P_i$  is determined empirically.” Applicant submits that the term “empirically” is well defined in the art. The scope of the claim is clear. The Office Action seems to suggest that the claim is broad. However, the breadth of a claim is not to be equated with indefiniteness. Therefore, Applicant respectfully requests that this rejection of Claim 5 be withdrawn.

Claims 6, 7 and 15 are rejected for allegedly being indefinite for reciting least squares, Cholesky decomposition and singular value decomposition methods. Applicant respectfully submits the recited methods are well known in the art and described in

numerous statistical and computational textbooks. They are frequently used to obtain empirical parameters using training data sets. The scope of the claims is clear to one of ordinary skill in the art. Therefore, this rejection of Claim 6, 7, and 15 should be withdrawn.

Claims 8, 9, 10, and 12-14 are directed to various refinement of the probe intensity prediction model. The scope of the claims is clear to one of skill in the art. The office Action seems to allege that the specification does not teach the claimed methods. Applicant respectfully submits that the various methods are described in, for example, page 24, of the specification. This rejection of Claims should be withdrawn.

In summary, the rejection of Claims 1-15 should be withdrawn. For the same reasons, the rejection of Computer Claims 45-59 should also be withdrawn.

#### Double Patenting

Claims 1 and 45 are provisionally rejected under the judicially created doctrine of obviousness-type of double patenting. Applicant would like to address this issue at a later date during the prosecution.

#### Claim Rejections – 35 USC § 102

Claims 1-15 and 45-59 are rejected under 35 USC 102(b) as allegedly being anticipated by Hacia et al. (1998) and Schutz et al. (1999).

Claims 1-15 and 45-59 are directed to computer implemented methods or computer software products for selecting probes for gene expression monitoring by predicting the intensity differences. Hacia et al. (coauthored by the inventor) does not teach the selection of probes for gene expression monitoring. Similarly, Schutz et al.

does not disclose the selection of probes for gene expression monitoring. The examples provided are related to genotyping applications and mutation detection.

Claims 1 and 45 are rejected under 35 USC 102(e) as allegedly being anticipated by Lange et al. USP 6,403,314, Santalucia et al (WO 01/94611 A2), Shannon et al (US 6,251,588), Wolber et al (USP 6,461,816), and Hyndman et al. Applicant respectfully disagrees and submits that the cited references fail to disclose “predicting hybridization intensities of a plurality of candidate probes and their corresponding control probe; and selecting the candidate probes that have the highest intensity difference over its corresponding control probe” All the cited references discuss predicting hybridization. They do not disclose the selection of candidate probes based upon intensity difference between the probes and their control probes. For example, Lange et al. discusses predicting thermostability of hybridization duplex using a matrix that weights the contribution of bases. Hyndman et al. discusses the selection of oligonucleotide probes pairs for PCR applications and for dot blots, Southern and Northern Blots (Pages 1093-1094). Probes are selected based upon their predicted  $T_m$  and specificity determined by searches against the GenBank (Table 1). There is no disclosure of selecting candidate probes that have the highest intensity difference. Since none of the cited references disclose every element of the claims, Applicant respectfully request that the rejection under 35 USC 102 be withdrawn.

### **CONCLUSION**

If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-

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5000. The Commissioner is authorized to charge any fees or credit any overpayments associated with this application to Deposit Account No. 01-0431.

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Respectfully submitted,

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